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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/978,632	11/25/1997	ELAZAR RABBANI	ENZ-53(C)	4638

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EXAMINER	
SCHULTZ, JAMES	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 09/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/978,632	RABBANI ET AL.	
	Examiner	Art Unit	
	J. D. Schultz, Ph.D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *246-253,255-262 and 264-270* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *246-253,255-262 and 264-270* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7 feb 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

Applicant's success in petitioning to revive the instant application following abandonment is noted. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after said petition. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 30 June 2005 has been entered.

Status of Application/Amendment/Claims

Applicant's response filed 30 June 2005 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 20 May 2002 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Objections

Claim 256 is objected to because of the following informalities: the phrase "both strand" is grammatically incorrect, and should be amended to read "both strands", if such is the intended recitation. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 249 recites the limitation "said sequence segment" in claim 248. There is insufficient antecedent basis for this limitation in the claim.

Claim 256 recites the limitation "said sequence segment" in claim 246. There is insufficient antecedent basis for this limitation in the claim.

Claims 261, and by dependency claim 262, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 261 requires the claimed construct to exhibit a "further biological activity", whereas no upstream activity for the claimed construct has yet been delineated.

Claim 264 recites the limitation "said ligand..." in claim 246. There is insufficient antecedent basis for this limitation in the claim. The remainder of this action presumes the dependency to be directed to claim 257, which is the only earlier claim which recites any type of ligand.

Claim 265 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 265 refers to "the construct of claim 263". However, claim 263 has been canceled. The remainder of this action presumes the dependency to be directed to claim 257, which is the only earlier claim which recites any type of ligand.

Claim 270 recites the limitation "said polynucleotide tale" in the construct of claim 248. There is insufficient antecedent basis for this limitation in the claim. It is presumed for the remainder of this action that the claim in tens to refer to the construct of claim 269, which is the immediately preceding claim that recites a polynucleotide tail.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 268 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

Claim 268 is drawn to a construct which when present in a cell produces a nucleic acid product, said construct being bound non-ionically to an entity comprising a chemical modification or a ligand in two or more locations on said construct.

It is not clear from a review of the specification as filed that the specification provides adequate support for the phrase "in two or more locations on said construct". Applicants arguments suggest only that all amendments are broadly supported by the disclosure as filed, and does not indicate with any specificity were any support for any such amendments might be. Furthermore, while the specification broadly discusses chemical modifications of nucleic acid

constructs, it is not clear where specific support might be had for a recitation of "two or more locations" within the context of the claimed invention. Should applicants disagree, applicants are invited to point out with specificity by page and line number where any such support may exist.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 246-253, 255-262, and 264-270 are rejected under 35 U.S.C. 102(a) as being anticipated by Overell et al. (WO 95/28494, applicants IDS of 7 February 2005).

The invention of the above claims is drawn to a chemically modified nucleic acid construct, wherein said construct comprises one of a modified nucleotide, a nucleotide analog, a non-nucleic acid entity, and a combination of the foregoing, wherein said construct directs the synthesis of a nucleic acid product having a biological activity, wherein said product is chosen from antisense RNA, antisense DNA, since RNA, ribozymes, mRNA, or a combination of these. The claims further direct that the construct be linear, circular, or branched, or that the construct be single-stranded, double stranded, partially double stranded, or triple stranded, or that the construct have a terminus which comprises a polynucleotide tail, which may be hybridized to a complementary polynucleotide sequence, or wherein the construct comprises DNA, RNA, a

hybrid thereof, a chimera thereof, or a combination. The claims also recite that the modified nucleotide may be chemically modified, or that the nucleotide analog be modified on the backbone or side chain, or both, or wherein the non-nucleic acid entity is attached to a single strand or both strands, or is a natural or synthetic polymer, or a natural or synthetic ligand, or a combination thereof, wherein the natural polymer comprises a modified or unmodified polypeptide, protein, polysaccharide, fatty acid, fatty acid ester, or a combination of the foregoing, or that the synthetic polymer comprises a homopolymer or heteropolymer which may carry either a net negative or net positive charge, wherein said construct exhibits a further biological activity imparted by said modification, which may be nuclease resistance, or cellular or nuclear localization, or a combination, wherein said ligand may be chosen from a single-stranded segment, a double stranded segment, a single-stranded construct tail, or a sequence complementary to a construct tale, or a combination of the foregoing, or wherein said ligand are macro molecules, small molecules, or a combination, or wherein said construct carries a net in a positive charge or a net negative charge or is neutral, or is hydrophobic, or wherein said construct comprises unmodified nucleotides and at least one nucleotide analog or non-nucleic acid entity, or wherein said construct produces a nucleic acid product said construct being bound non-ionically to an entity comprising a chemical modification or ligand in two or more locations on said construct which may also have a polynucleotide tail which may also be hybridized to a complementary polynucleotide sequence.

At the outset it is noted that claims 255-260, 264, and 265 recite limitations of elements from the broad claim, wherein said elements are stated in the alternative. Accordingly, because such elements are stated in the alternative, and because all limitations of the broad claim are read

into the later depending claim, art that teaches one element is considered to reject the entire claim, even in later dependant claims which limit alternative elements that are not taught in the art, because those elements are not excluded in the claim language of the broad claim. For example, broad claim 246 recites nucleic acid constructs comprising A) a modified nucleotide, OR B) a nucleotide analog, OR C) a non-nucleic acid entity. Claim 255 recites the construct of claim 246, wherein at least one of said nucleotide analogs have been modified on the backbone or side chain. However, because all claim limitations of the broad claim 246 are read into claim 255, and because claim 255 does not specifically exclude the elements of modified nucleotide or non-nucleic acid entity elements of claim 246, art directed to the modified nucleotide or non-nucleic acid entity elements of claim 246 is also considered to anticipate claim 255.

Overell et al. teach a gene delivery fusion protein construct which bind to vectors to enhance transduction efficiency. Thus, Overell et al. teach a chemically modified nucleic acid construct, which is the vector bound to a fusion protein which is a non-nucleic acid entity, wherein said construct directs the synthesis of a nucleic acid product having a biological activity, wherein said product is chosen from sense RNA, that is circular, or that is double stranded, and that has a terminus which comprises a polynucleotide tail, which may be hybridized to a complementary polynucleotide sequence, and wherein the construct comprises DNA. Overell et al. also teaches wherein said non-nucleic acid entity is attached to a single strand or double strand and to a natural or synthetic polymer, which is a polypeptide, which is a heteropolymer. Overell et al. is considered to teach the limitations of claims 264 and 265 because these claims do not limit the nucleic acid entity for reasons provided above. Overell et al. is considered to teach that said construct is hydrophobic, or wherein said construct comprises unmodified

nucleotides one non-nucleic acid entity, and wherein said construct produces a nucleic acid product, and said construct is considered to be bound non-ionically to an entity comprising a chemical modification in two or more locations on said construct. Finally, Overell et al. is considered to teach such constructs which comprise a polynucleotide tail which may also be hybridized to a complementary polynucleotide sequence.

Claims 246-253, 255-262, and 264-270 are rejected under 35 U.S.C. 102(b) as being anticipated by Vos et al.. (Mol. Cell. Biol. 1989, 9(7)2897-2905).

The invention is as discussed above.

Vos et al. teaches a plasmid which has been chemically cross-linked with HMT. Vos et al. teaches that HMT cross links the plasmid which enhances its chromosomal integration efficiency. Vos et al. is thus considered to teach a chemically modified nucleic acid construct, which is the cross-linked vector which Vos comprises modified nucleotides, wherein said construct integrates into the chromosome and thus directs the synthesis of a nucleic acid product having a biological activity, wherein said product is chosen from DNA, that is circular, and that is double stranded, and that has a terminus which comprises a polynucleotide tail, which may be hybridized to a complementary polynucleotide sequence. Vos et al. also teaches wherein said modified nucleotide is attached to a single strand or both strands which is a natural or synthetic polymer, which is a cross-linked plasmid, which is a heteropolymer. Vos et al. is considered to teach the limitations of claims 255-260, 264 and 265 because these claims do not limit the modified nucleotide for reasons provided above. Vos et al. is considered to teach that said construct has an overall net positive or negative charge or is hydrophobic, and wherein said

construct comprises unmodified nucleotides and at least one nucleotide analog, and wherein said construct produces a nucleic acid product which is the chromosome, and wherein said construct is considered to be bound non-ionically to an entity comprising a chemical modification in two or more locations on said construct. Finally, Vos et al. is considered to teach such constructs which comprise a polynucleotide tail which may also be hybridized to a complementary polynucleotide sequence.

Conclusion

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Douglas Schultz, Ph.D. whose telephone number is 571-272-0763. The examiner can normally be reached on 8:00-4:30 M-F.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached at 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service

center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

JD Schultz, PhD

J.D. SCHULTZ, Ph.D.
PATENT EXAMINER